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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,976	03/26/2004	Won-Bin Young	P05768US01	9933

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EXAMINER	
RIGGINS, PATRICK S	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,976	YOUNG ET AL.	
	Examiner	Art Unit	
	Patrick S. Riggins	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48,49 and 51-73* is/are allowed.

6)☒ Claim(s) *1-47 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: The Saha and Weeratna references of page 2 are incorrectly referenced.

Appropriate correction is required.

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. These are particularly noted on pages 18 and 31.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

4. According to 37 C.F.R 1.821 any peptide sequence of greater than four amino acids must appear in the sequence listing. Page 38 discloses the sequences of both the c-*myc* and FLAG epitope tags. As they are both straight unbranched chains of greater than four amino acids, they must appear in the sequence listing. Appropriate correction is required.

Claim Objections

5. Claims 12-14, 16-17, and 26-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In all cases, the claims intend to broaden the scope of the claims from which they depend. For example, claim 10 is limited to a method where the construct comprises two restriction sites at both the 5' and 3' ends of the marker exon, while claim 12 attempts to broaden the scope such that the construct can comprise only the two restriction sites at the 5' end of the marker exon.

6. Applicant is advised that should claim 27 be found allowable, claim 28 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112-1

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 74 and 75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. These claims are drawn to two specific plasmid vectors, pGT13 and pGTfso-M. As these specific plasmids would have unique junction regions and unique regions of overlap, the skilled

artisan would require either specific instructions on what restriction enzymes were used and the nature of the ligation steps or the full nucleotide sequence of the vectors, with the possibility that the sequences overlaying the junction regions may have been sufficient. The components to construct the plasmids are indeed available to the skilled artisan, but absent the instructions on which restriction sites were used or which PCR primers were used if PCR steps were required for construction, the skilled artisan would in no way be assured that the plasmids constructed from the available components would have identical junctional regions between the components. As such, the specification fails to teach the skilled artisan how to make the two plasmids of the invention.

10. A deposit of the appropriate biological material to make the plasmids readily available to the skilled artisan would be acceptable for overcoming this enablement rejection. To ensure full compliance refer to 37 C.F.R 1.801-1.809.

Claim Rejections - 35 USC § 112-2

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-47 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: in independent claim 1, 10, 24, 36, 38, and 40 an mRNA isolation step is required to link the first portion of the claim describing the structure of the introduced constructs to the method steps that follow, starting with the step of "reverse transcribing the isolated mRNA." Claim 1 additionally requires a step that is missing prior to the

step of "self-ligating the cDNA fragment." As a type IIs restriction enzyme cuts outside of the non-palindromic recognition site and generally cuts leaving an overhang, the nature of the overhang is unknown, as the construct is specifically designed to cut within the unidentified, adjacent exons, it is highly unlikely that the two overhangs would have compatible cohesive ends. To successfully achieve self-ligation, the unidentified cohesive ends must first be filled in to create blunt ends. Only after this step would self-ligation even be possible. Claims 10, 24, 38, and 40 further lack essential elements pertaining to the linkers to be ligated to the type IIs cleaved fragments. For the practice of the invention it is essential that the linkers comprise a restriction site for later cleavage steps and that the linkers comprise an appropriate number of randomized overhang nucleotides to allow for ligation of the liners to the unidentified overhangs produced by the type IIs enzymes.

13. Claims 1-47 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claims 1, 10, 24, 36, 38, and 40 recite the limitation "the isolated mRNA". There is insufficient antecedent basis for this limitation in the claims. If the additional step of isolating the mRNA were added to the claims as required above, this would correct this antecedent basis problem.

15. Claims 1, 10, 12-14, 24, 26-28, 36, 38, and 40 all recite, when referring to the two restriction sites at both the 5' end and the 3' end, that "at least one of the RER sites is recognized by a Type IIs restriction enzyme." This is vague and indefinite because it implies that the other RER site could also be a Type IIs enzyme. This would neither be desirable not effective. The

second RER sites are present to allow for the cleavage of the PCR product to generate "a linear DNA fragment containing upstream and downstream exon tags fused in an inverted conformation". This then allows either the insertion of the fragment into a sequencing vector, or for concatamerization prior to insertion into a sequencing vector. For either of these to successfully take place the overhangs produced must be known and have an appropriate cohesiveness. As a Type IIs enzyme leaves overhangs that would differ for almost any two different Type IIs recognition sites they would not be an effective choice for the second RER site present at each end of the marker. To delete the term "one of" in each of these cases would be remedial.

16. Claim 10 recites the limitation "subjecting the cDNA to a Type IIs restriction enzyme that recognizes one of the Type IIs RER sites located at the 5' end of the marker exon". This is vague and indefinite because it is unclear what is fully intended by this limitation as only one Type IIs restriction site has been identified previously at the 5' end. To delete "one of" would be remedial. Claim 10 further recites the limitation "subjecting the amplification products to one or more restriction enzymes that recognize the RER sites not previously recognized by the Type IIs restriction enzymes." This limitation should recite something along the lines of --subjecting the amplification products to one or more restriction enzymes that recognize the RER site not previously recognized by the Type IIs restriction enzymes and that recognize the RER site present in the ligated linker sequence--. Although as currently drawn this claim limitation would lack antecedent basis due to the thus far unrecited RER site in the linker, but correction of the linker description deficiency would negate this antecedent basis issue. Claims 24, 38, and 40 have these same issues.

17. Claims 36, 38, and 40 recite the limitation "the polynucleotide construct" in line 3. There is insufficient antecedent basis for this limitation in the claims.

18. Claim 36 is vague and indefinite because it recites "RNA tags". It is unclear what is intended by this limitation as the tags in question are not composed of RNA, but instead consist of cDNA. Thus the skilled artisan would be unable to determine the metes and bounds of this claim limitation.

19. Claims 9, 23, and 35 recite that the fluorescent protein will be "measured by fluorescence activated flow cytometry." This is unclear because "fluorescence activated flow cytometry" is not an art-recognized term. The art-recognized terms are either --fluorescence-activated cell sorting--, or --flow cytometry--. It would seem that in the instant case, the appropriate term would be to recite --flow cytometry--. As the utilized term is not art-recognized, the skilled artisan would be unable to determine the metes and bounds of this claim limitation.

20. Claim 50 recites that the polynucleotide construct further comprises "a positive selection marker". This is unclear because the specification only teaches of the use of a positive selection marker, such as GFP, as the marker exon and a negative selection marker, such as neomycin resistance, downstream of the marker exon cassette. Thus, in light of the specification, the skilled artisan would be unclear about the metes and bounds of this limitation since the disclosure only seems to teach the placement of a negative selection marker downstream of the marker exon not a positive selection marker. To change "positive selection marker" to --negative selection marker-- would be remedial.

Conclusion

21. Claims 48, 49, 51-73 are allowable. Claims 1-47, 50, 74, and 75 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick S. Riggins whose telephone number is (571) 272-6102. The examiner can normally be reached on M-F 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick Riggins, Ph.D.
Examiner
Art Unit 1636

JAMES KETTER
PRIMARY EXAMINER